Acute Kidney Injury in the Tropics

By

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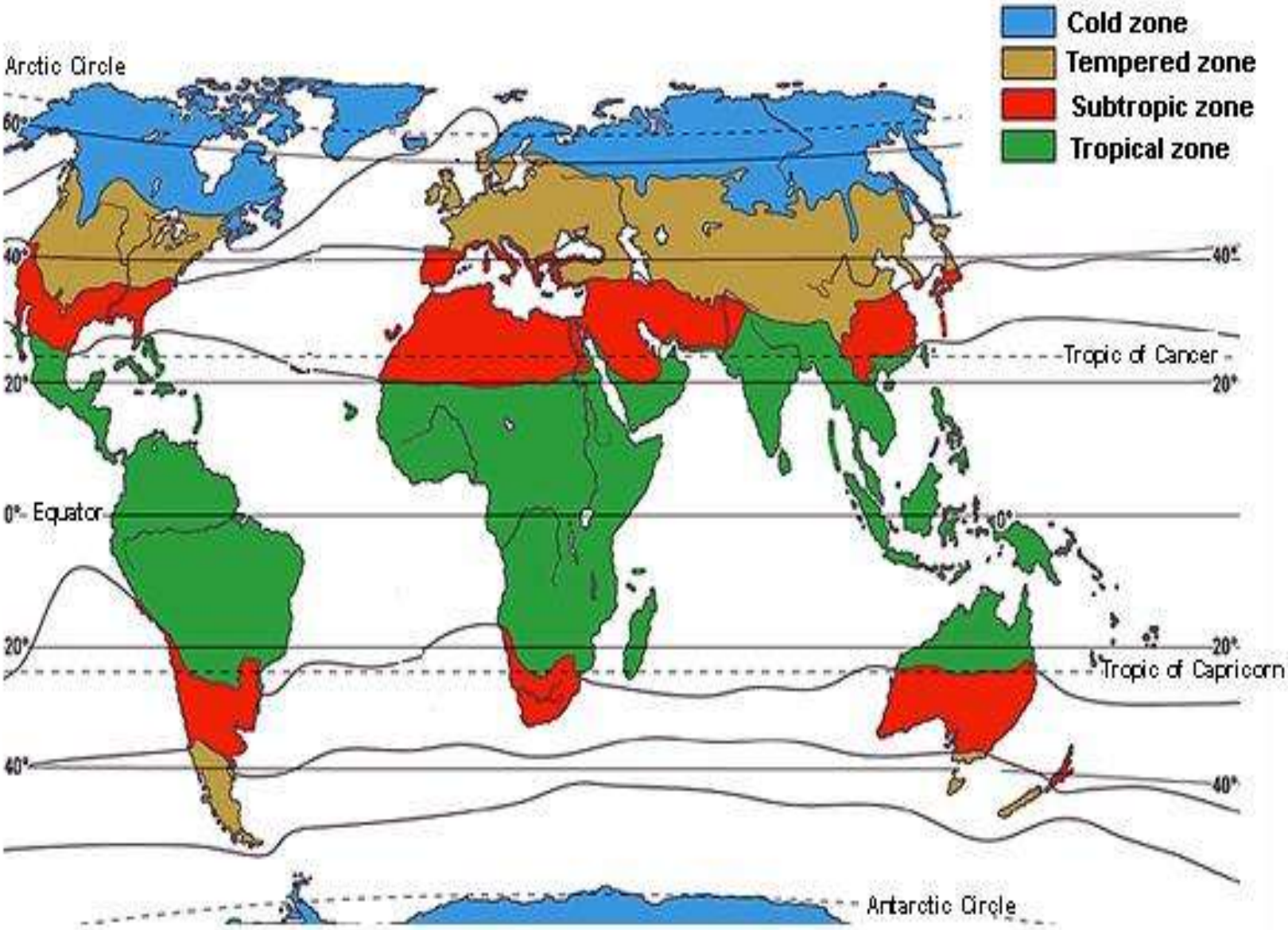
What is tropics?

The **tropics** is a region of the earth surrounding the equator. It is limited in latitude by the tropic of Cancer in the northern hemisphere at 23° N and the tropic of Capricorn in the southern hemisphere at 23° S.


Cold zone
Tempered zone
Subtropic zone
Tropical zone
Arctic Circle
60°
40°
20°
0° Equator
20°
40°
40°
20°
0°
20°
40°
Tropic of Cancer
Tropic of Capricorn
Antarctic Circle

Why tropics?

- Particular infections.
- consumption of unsafe drinking water.
- Use of natural medicines.
- Exposure to environmental toxins.
- Poverty.
- Malnutrition.
- lack of an adequate sanitary infrastructure and public health system.

What is the difference between AKI in tropics and that in temperate zones ?

- In contrast to trauma, industrial accidents, drugs, cardiogenic shock and renal transplantation rejection being the common causes of AKI in the developed world, acute tubular necrosis (ATN) due to community-acquired infections remains the commonest cause in the tropics.

- The relatively younger age of patients in the tropics. In contrast to the old mean age of patients with AKI in the temperate zone.

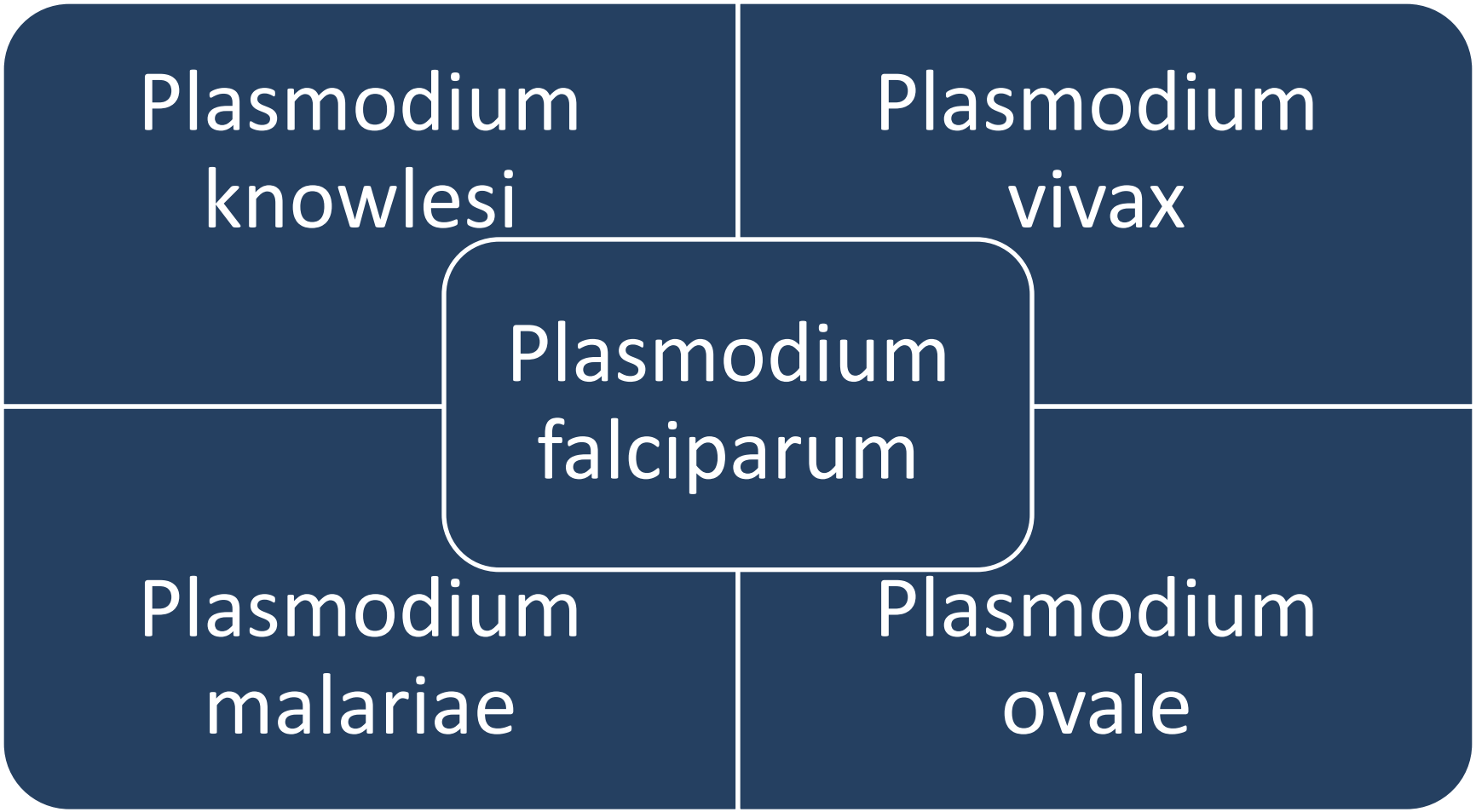
- The gross inadequacy of treatment facilities in the tropics.

Causes of AKI in the Tropics

Infections (sepsis)	Plant toxins	Poisons	Miscellaneous
Falciparum malaria Leptospirosis Typhoid Hemorrhagic fevers Infective diarrhea HIV Zygomycosis Melioidosis Scrub typhus Chlamydia Legionnaires disease Epidemic Rift Valley fever	Mushroom Herbal medicine Djenkol beans Propolis Cleistanthus collinus Triperygium wilfordii	**Animal poisons** Snakebites Wasp, hornet, bee sting Scorpion sting Spider bite Jellyfish sting Carp gallbladder or bile **Chemical** Copper sulfate Ethylene glycol Ethylene dibromide Chromic acid Paraquat Formic acid	G6PD deficiency Heatstroke Natural disasters Hemolytic uremic syndrome Acute glomerulonephritis Surgical ARF Obstetric ARF Acute cortical necrosis Trauma

MALARIA

MALARIA; species



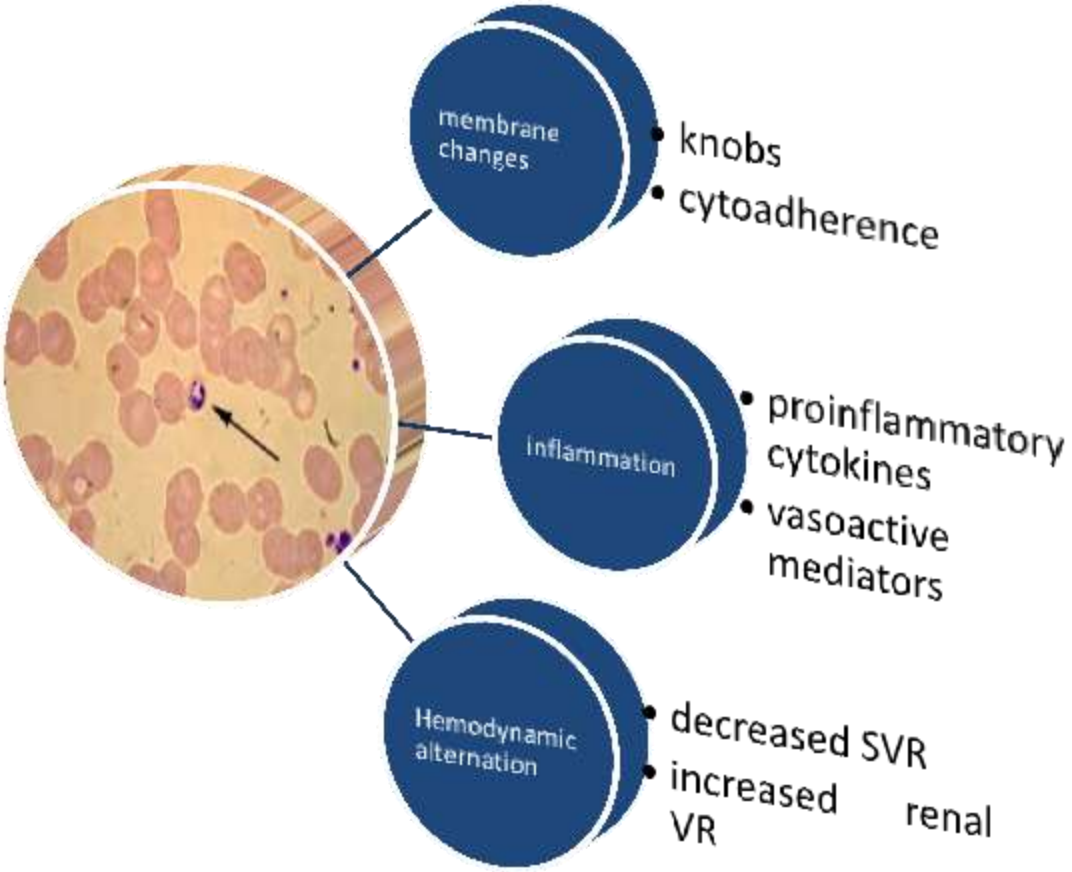
MALARIA; epidemiology

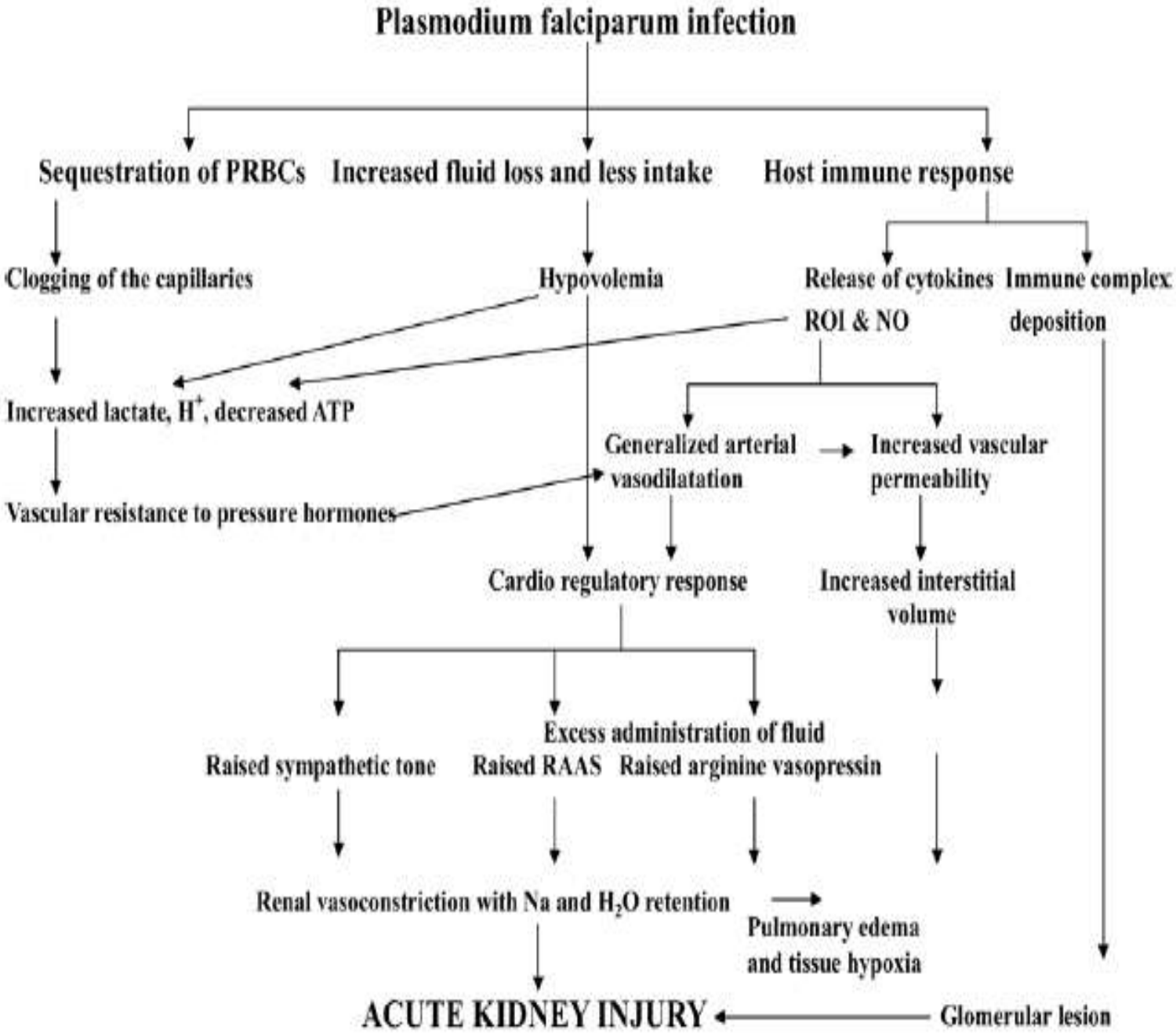
- The WHO estimated that globally malaria affects more than 200 million patients annually with nearly 1 million deaths.

- The contribution of malaria as the cause of AKI ranges from 2% to 39%.

- The incidence of AKI in P. falciparum malaria can be as high as 60%.

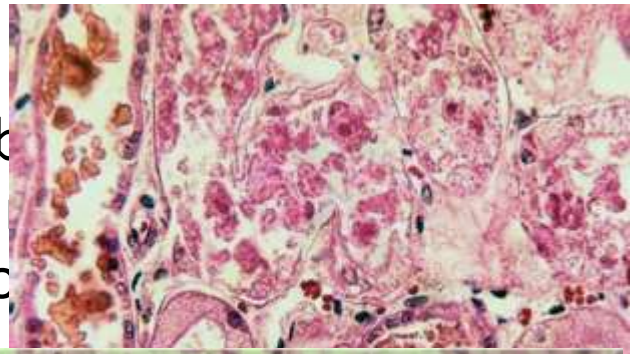
MALARIA; Pathophysiology



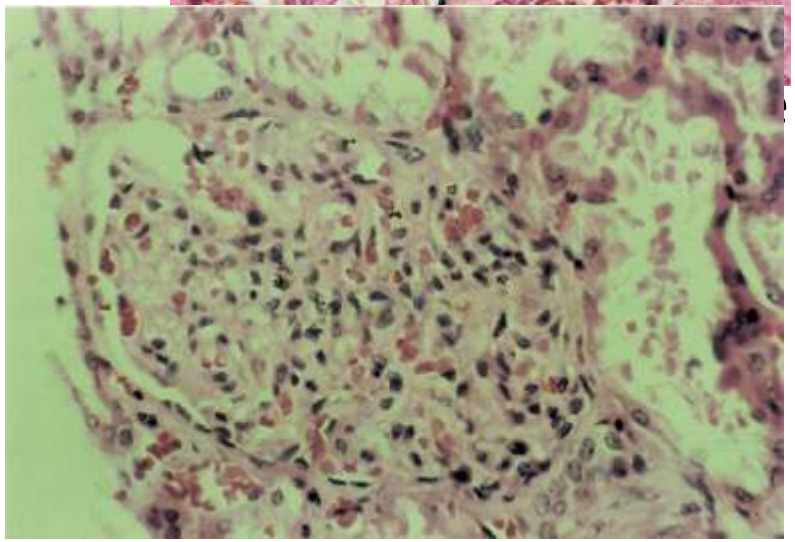

Plasmodium falciparum infection
Sequestration of PRBCs
Increased fluid loss and less intake
Host immune response
Clogging of the capillaries
Hypovolemia
Release of cytokines
Immune complex deposition
ROI & NO
Increased lactate, H+, decreased ATP
Generalized arterial vasodilatation
Increased vascular permeability
Vascular resistance to pressure hormones
Cardio regulatory response
Increased interstitial volume
Excess administration of fluid
Raised sympathetic tone
Raised RAAS
Raised arginine vasopressin
Renal vasoconstriction with Na and H2O retention
Pulmonary edema and tissue hypoxia
ACUTE KIDNEY INJURY
Glomerular lesion

MALARIA; Pathology

- Ischemic and hypoxic AKI with tubular changes vary from cloudy swelling to tubular degeneration.



- Immune complex GN is usually ob
  deposition of C3, IgM, and malarial a
  area and *in situ* immune complex depo



- Interstitial mononuclear infilt
  observed.

- Thrombotic microangiopathy ha

MALARIA; Clinical Manifestations

- Constitutional symptoms.

- Jaundice may be present.

- electrolyte changes are common:

✓ Hyponatremia 67%

✓ Hypokalemia 20-40%

✓ Hypocalcemia 45%

✓ Hypophosphatemia 6-30%

✓ Hypomagnesemia 30%

MALARIA; Clinical Manifestations

- Severe acidosis, hypoglycemia, and central nervous system symptoms can be observed.

- Rapid increase in BUN and serum creatinine.

- Urine analysis:

✓ Few erythrocytes, leukocytes, granular casts and mild proteinuria.

✓ Hemoglobinuria.

✓ Myoglobinuria

MALARIA; Treatment

- Antimalaria Drugs:

  Quinine for 7 days.

- Maintenance of fluid and electrolyte levels:

  Fluid should be given cautiously.

- Renal replacement therapy:

  Intermittent hemodialysis (daily or alternate day), CVVH, or CAVH.

- Management of complications:

  As pneuomonia.

SNAKEBITES

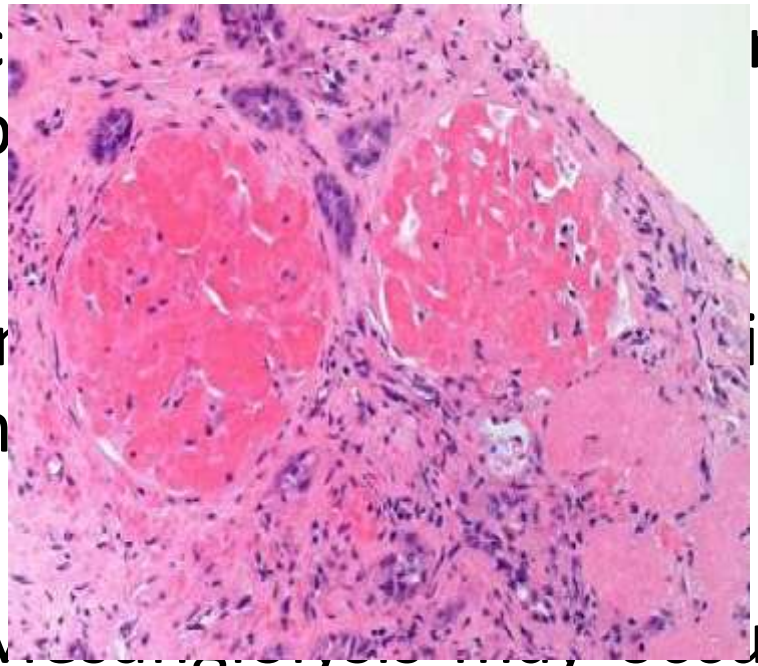
SNAKEBITES; Pathogenesis

Enzymes, toxins, and peptides

- Renal vasoconstriction
- Hypovolemia, hypotension, depression of the medullary vasomotor center or the myocardium
- Intense inflammatory mediator release, induction of oxidative stress
- Hemolysis, altered fibrinolysis, myoglobinuria, or disseminated intravascular coagulation
- Direct nephrotoxicity

SNAKEBITES; Pathology

- Acute tubular cell injury ranging from mild c r ne e or p



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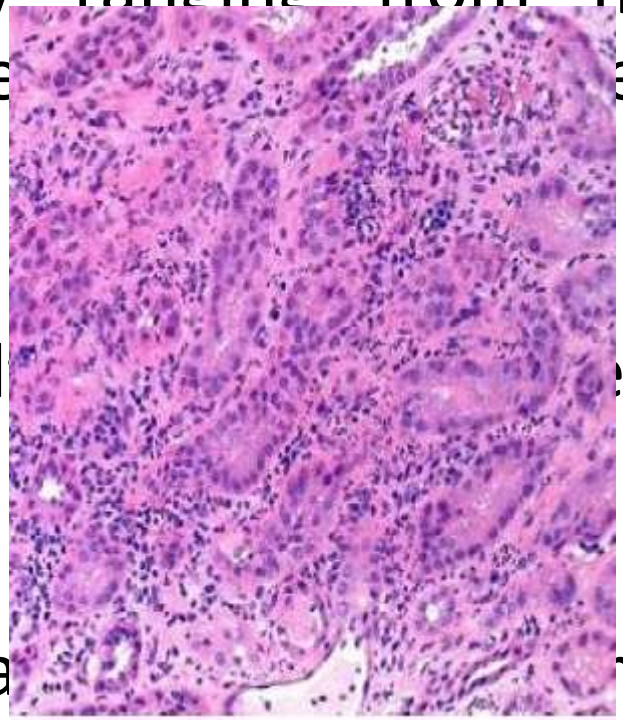

- M ur, a may show fibrin thrombi.

SNAKEBITES; Clinical Features

- Local pain, swelling, blistering, ecchymosis, and tissue necrosis.

- The commone tation in accidents involving these tion abnormalities leading to blee

- Muscle paralysis and rhabdomyolys

SNAKEBITES; Clinical Features

- AKI develops within a few hours to as late as 96 hours after the bite.

- AKI is usually oliguric and catabolic, with rapidly rising levels of BUN, serum creatinine, and potassium.

- Oliguria generally lasts for 1 to 2 weeks, and its persistence suggests the likelihood of acute cortical necrosis.

SNAKEBITES; Clinical Features

Laboratory investigation may show:

- Hemolysis (elevated free plasma hemoglobin, LDH and reduced haptoglobin).
- Hypofibrinogenemia.
- Reduced factors V, X, and XIIIa, protein C, and antithrombin; and elevated FDP.
- Rhabdomyolysis may be indicated by raised CPK.
- Cola-colored urine is noted in patients with hemolysis or rhabdomyolysis.

SNAKEBITES; Management

- Early administration of specific monovalent antivenom.
- Appropriate volume replacement, maintenance of good urine flow, urinary alkalization in patients with rhabdomyolysis, correction of electrolyte imbalance.
- Administration of tetanus immunoglobulin, and treatment of infections.

LEPTOSPIROSIS

LEPTOSPIROSIS

- It is caused by *Leptospira* genus spirochetes.
- The infection is transmitted to humans through animal urine.
- Human cases range from 10 to 100 per 100,000 population per year in the humid tropics.

LEPTOSPIROSIS

- *Leptospira interrogans* endotoxins affect the tubulointerstitial cells. Glomerular changes are usually not relevant.

- The bacterial outer membrane contains lipopolysaccharide (LPS), cytotoxic glycolipoprotein (GLP) and lipoprotein (LipL).

- The effect of GLPs on tubular Na_+-K_+-ATPase activity is potentially involved in AKI cellular pathophysiology. in the urinary concentrating defects, and in the paradoxical hypokalemia frequently seen in these patients.

LEPTOSPIROSIS

- Oliguria, jaundice, and arrhythmias have been shown to be predictors of AKI development.

- Antibiotic treatment is considered efficient in the disease early and in the late and severe phases.

- Treatment recommendations include a high dialysis dose, conservative fluid intake, and approaches to minimize lung injury, such as low tidal volume and high positive end-expiratory pressure, when artificial ventilation is required.

NATURAL MEDICINES

NATURAL MEDICINES

- Herbs are used extensively in poor societies living in the tropics.
- AKI has been described in association with several natural herbs.
- About 25% to 35% of all AKI from medical causes in African hospitals are related to herbal remedies.

Pathogenesis of Natural Medicine–Induced Acute Kidney Injury

- Several factors affect the toxicity and likelihood of kidney injury:

- Incorrect identification may lead to substitution of a medicinal plant with a toxic one.
- Incorrect methods of preparation or use.
- potentially nephrotoxic exogenous substances such as soap, vinegar, copper sulfate, and potassium permanganate are often added to the plant extracts.

Herbal Causes of Acute Kidney Injury in Tropical Countries

Plant (Common or Local Name)	Country	Active Molecule	Renal Manifestations	Other Manifestations
Averrhoa bilimbi (irumban puli)	South India	Oxalic acid	Intratubular obstruction	
Caillilepis laureola (impila)	Sub-Saharan Africa	Atractyloside		
Catha edulis (khat leaf)	East Africa, Arabian peninsula	*S*-cathinone and ephedrine		
Cleistanthus collinus (oduvan)	India	Cleistanthin A and B, collinusin, and diphy		
Colchicum autumnale (autumn crocus)	Turkey	Colchicine		
Crotalaria laburnifolia (bird flower)	Zimbabwe, Sr Lanka			
Dioscorea quartiniana (yam)	Africa, Asia			
Pithecellobium lobatum and *Pithecellobium jiringa* (djenkol beans)	South East As			
Dodonaea angustifolia (sand olive)	South Africa			
Euphorbia me (spurge)				
Larrea trident		Nordihydroguaiaretic and S-quinone		
Propolis resin		Unknown		
Rhizoma rhei		Anthraquinones (emo aloe-emodin)		
Securidaca lo (violet tree		Methylsalicylate, securinine, saponins		
Sutherlandia brush)		Unknown	Acute interstitial nephritis	Pulmonary embolism
Takaout roumia	Morocco, Sudan	Paraphenylenediamine	Acute tubular necrosis	Rhabdomyolysis
Semecarpus anacardium (marking nut)	India	Unknown	Acute tubular necrosis and acute cortical necrosis	Corrosive blisters in pharynx, gastrointestinal irritation, shock, coma
Taxus celebica (Chinese yew)	Asia	Flavonoid	Acute tubular necrosis and acute interstitial nephritis	Hepatitis, hemolysis, DIC
Thevetia peruviana (yellow oleander)	India, Sri Lanka	Cardiac glycosides	Acute tubular necrosis	Liver failure, cardiac arrhythmias
Tripterygium wilfordii (thunder god vine)	Taiwan	Triptolide	Acute tubular necrosis	Diarrhea, shock
Uncaria tomentosa (cat's claw)	Peru	Alkaloids and flavonols	Acute tubular necrosis	Diarrhea, hypotension, bruising, bleeding gums

EBOLA

EBOLA; Clinical Manifestations

- Incubation period of 2 to 21 days.
- Flu-like syndrome.
- A macropapular rash associated with varying severity of erythema and desquamate can often be noted by day 5 - 7 of the illness.

EBOLA; Clinical Manifestations

- Hemorrhagic manifestations arise during the peak of the illness and include petechiae, ecchymoses, uncontrolled oozing from venepuncture sites, and mucosal hemorrhages.

- Hypotension, hypovolemia and DIC.

- Diagnosis by: throat swab or skin biopsy, PCR, or ELIZA.

EBOLA; Treatment

- Symptomatic and supportive care.
- Zmapp: effective in animal studies, but still no randomized controlled trials in human.
- Antiviral drugs: (such as Ribavirin and lamivudine) no survival benefit.
- Vaccine: 2 vaccines still under investigation.

EBOLA; Treatment

Investigational modalities and vaccines for Ebola virus disease treatment.

Drug	Mechanism	Effect
Zmapp	Combined antibody binds to and inactivates virus	Protects monkeys infected with Ebola virus Seven people on "compassionate use", two died
Convalescent therapy	Passive immunization (neutralizing antibodies, serum from recovered Ebola patients)	Protective effect, *in vitro* Therapeutic effect, in rodents but fails in non human primates
Antiviral drug		
Ribavirin	Interferes with capping of viral mRNA	Not recommended due to severe adverse effects
Lamivudine	A nucleoside analogue that interferes gene replication	No survival benefit demonstrated in EVD
Favipiravir	Broad effect antiviral compound that inhibits a viral enzyme	Protects mice with Ebola. Phase III trials in human with influenza
Vaccine		
cAd3	Segments of genetic material from two Ebola virus species delivered by a chimpanzee virus	Imminent phase I clinical trials
rVSV	A gene from Ebola loaded in a weakened version of vesicular stomatitis virus	Prevents lethal infection in non human primates

EBOLA; Treatment

Successful Delivery of RRT in Ebola Virus Disease

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ABSTRACT

AKI has been observed in cases of Ebola virus disease. We describe the protocol for the first known successful delivery of RRT with subsequent renal recovery in a patient with Ebola virus disease treated at Emory University Hospital, in Atlanta, Georgia. Providing RRT in Ebola virus disease is complex and requires meticulous attention to safety for the patient, healthcare workers, and the community. We specifically describe measures to decrease the risk of transmission of Ebola virus disease and report pilot data demonstrating no detectable Ebola virus genetic material in the spent RRT effluent waste. This article also proposes clinical practice guidelines for acute RRT in Ebola virus disease.

EBOLA; Treatment

Parameter	Clinical Guideline
Modality	CRRT recommended for initial treatment
	Consider transition to PIRRT (using same CRRT equipment) for continued RRT until patient either (*1*) recovers renal function or (*2*) is capable of leaving biocontainment isolation (*i.e.*, negative viral PCR studies in blood)
Staff	If possible at the institution, all patients should receive RRT using CRRT equipment by extensively trained ICU nurses as primary clinical nurses at bedside
	Minimize additional staff entry in the biocontainment environment (*i.e.*, specialty dialysis nurses)
Access	Temporary nontunneled dialysis catheter placed at bedside under direct ultrasound visualization. Extra precautions should be taken to contain bloody waste from this procedure
	The right internal jugular vein is the preferred access site (with the left internal jugular vein as the backup site), given that this presents the lowest bleeding risk because patients with EVD may experience bleeding diatheses. Recommend that subclavian insertion sites be avoided
	Unless portable chest imaging after access insertion is unavailable, femoral access sites should be avoided secondary to bleeding risks (retroperitoneal bleeding)
	Consider use of nonreflux dialysis grade caps for dialysis vascular access
CRRT dosing	No EVD-specific dosing needs. Consistent with Kidney Disease Improving Global Outcomes statements, support target CRRT dose to deliver a total effluent dose of 20–25 ml/kg per hour[10] unless higher dosing is needed to augment small solute and electrolyte clearance or correction of acidemia
Anticoagulation	RCA is preferred and recommended in all patients to extend filter life and reduce potential staff exposures with filter exchanges
Effluent disposal	CRRT effluent has a low infectious risk, but because it is handled in an EVD-positive area and a small dialyzer leak may be undetected, recommend that effluent be treated as hazardous and disposed of in a similar manner as individual institution/local guidelines require for disposal of other bodily fluids in EVD[11]
Nutrition support during CRRT	Ensure that patients receive appropriate augmented nutrition support while receiving CRRT as recommended by clinical guidelines (total daily protein intake of approximately 2 g/kg per day)[24,25]

THANK YOU